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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/260,468	03/02/1999	JAMES ROBL	000270 - 057	6587

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EXAMINER

WOITACH, JOSEPH T

ART UNIT PAPER NUMBER

1632

DATE MAILED: 05/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Advisory Action

Application No.
09/260,468

Applicant(s)
Robl, J. et al.

Examiner
Joseph T. Weitach

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1632



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Apr 24, 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on Nov 20, 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attached.

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: 1, 2, 4-19, 21-25, and 32-57

Claim(s) withdrawn from consideration: 26-30

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s).

10. ☐ Other:

Deborah Crouch
DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 1632

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Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Voitach** and the group art unit is now **1632**.

Section 2(a):

Proposed amendments to claim 1 are drawn to new and specific steps not previously considered. The previous claims encompassed 'culturing' the NT unit, and the new step of 'disassociating' can involve various methodology which have effects on the resulting isolated cells, raising new issues under 35 USC 112, first paragraph, and requires new search and considerations for 35 USC 102/103 rejections. Newly proposed claims 58-61 raise 35 USC 112, first and second paragraph, issues. Specifically claim 1 requires only a two-cell NT, and it is unclear what the inner-most portion of a two cell NT would be, and ultimately depends on how the NT unit is cultured. Claim 1 encompasses the use of an oocyte and nuclear material from any species, and thus encompasses human nuclear material and a primate oocyte, however this specific combination was not previously claimed nor do pending dependent claims specifically recite this combination (claims 55 and 56 encompassed ungulate and bovine). The new specific combination of human nuclear material and primate oocyte would require a new search and consideration for both 35 USC 112, first paragraph and 35 USC 102/103.

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Section 5(c):

101 rejection

Applicants argue that post-filing art demonstrates that mitochondrial DNA is maintained in cloned animals generated by nuclear transfer methods. Further, Applicants argue that this observation is consistent with normal fertilization wherein the sperm mitochondria is eliminated during embryogenesis. Citing *Diamond v. Chakrabarty*, Applicants argue that the embryonic stem-like cell instantly claimed can only be a product of human intervention. Applicants' arguments have been fully considered.

Examiner concedes that post filing art supports that nuclear transfer methodology may result in an embryo which contains both maternal and paternal mtDNA, however heteroplasmy as seen in Dolly, was the result of same species nuclear transfer. Additionally, Examiner would note that the art supports that heteroplasmy can occur between subspecies (see for example Shitara *et al.* Genetics 156:1277-1284 and Meirelles *et al.* Genetics 158:351-356). However, this phenomena does not necessarily extend to every mammalian (or animal) species or to all cell types used for nuclear material (see Shitara *et al.*). Further, the art clearly suggests that xenomitochondrial cybrids can be generated, however due to incompatibilities and the inability of the cybrid to develop the cross-species reconstituted embryos fail to develop. Therefore, even if the instantly claimed methods did result in an embryo and/or stem-like cells derived from said embryo, the art would strongly suggest that the mitochondria present in the viable embryonic stem-like cells would be from the same species as the donor, i.e. compatible. Further, it should

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be noted that neither the process nor the resulting embryo exclude the presence of donor mitochondria, and thus the product claims would clearly comprise embryos with only donor mtDNA, *i.e.* not heteroplasmic, and therefore not reflect the hand of man.

112 rejection

Applicants argue that the specification provides adequate guidance for use of the resulting ES-like cells besides transplantation. Applicants point to the specification for support in the use of the cells for *in vitro* models for differentiation. Further, Applicants point to 'the gaur data previously submitted demonstrates that cross-species nuclear transfer nuclear transfer may be used to generate differentiated cells' and that such cells may be useful (Applicants amendment, middle of page 5). Additionally, in attempt to more clearly set forth the pluripotency of the instantly resulting and claimed embryonic like cells, amendments to the claims have been made to indicate more clearly the nature of the resulting cell. Finally, it is argued that once the cells are made, the use of the cells may be adapted to methods known in the art.

Examiner notes that other potential uses are literally supported by the disclosure, however it is unclear what model of differentiation would be supported by this suggestion. If the cells represent unique cell types not found in nature, they would not represent any cell suitable for generating a model system. The specification fails to provide what specific types of models would be generated and what methodology would be used or what types of conclusions one would draw from experiments done in such a model system. Additionally, the data in the instant

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specification indicates that the cells generated by methods encompassed by the claimed methods consistently do not divide beyond 4-16 cell stage (Table 1). Further, evidence for the ability of a cell to simply differentiate does not provide any the necessary guidance on how to use said cell or what model it represents. Applicants' arguments that methods known in the art could be adapted for use of the instantly claimed method are unpersuasive because the disclosure does not provide the necessary guidance on what methods one would or should adapt for use of the cells, or how to specifically adapt said methods.

102 rejection

Applicants' arguments are directed to claim amendments which have not been entered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Joseph T. Woitach